

Response of Human Prostate Cancer Cells to Mitoxantrone Treatment in Simulated Microgravity Environment

Ye Zhang^{1,2}, Christopher Edwards³, and Honglu Wu¹

¹ NASA-Johnson Space Center, Houston, TX

² Wyle Integrated Science and Engineering Group, Houston, TX

³ Oregon State University, Corvallis, OR

This study explores the changes in growth of human prostate cancer cells (LNCaP) and their response to the treatment of antineoplastic agent, mitoxantrone, under the simulated microgravity condition. In comparison to static 1g, microgravity and simulated microgravity have been shown to alter global gene expression patterns and protein levels in various cultured cell models or animals. However, very little is known about the effect of altered gravity on the responses of cells to drugs, especially chemotherapy drugs. To test the hypothesis that zero gravity would result in altered regulation of cells in response to antineoplastic agents, we cultured LNCaP cells for 96 hr either in a High Aspect Ratio Vessel (HARV) bioreactor at the rotating condition to model microgravity in space or in the static condition as a control. 24 hr after the culture started, mitoxantrone was introduced to the cells at a final concentration of 1 μ M. The mitoxantrone treatment lasted 72 hr and then the cells were collected for various measurements. Compared to static 1g controls, the cells cultured in the simulated microgravity environment did not show significant differences in cell viability, growth rate, or cell cycle distribution. However, in response to mitoxantrone (1 μ M), a significant proportion of bioreactor cultured cells (30%) was arrested at G2 phase and a significant number of these cells were apoptotic in comparison to their static controls. The expressions of 84 oxidative stress related genes were analyzed using Qiagen PCR array to identify the possible mechanism underlying the altered responses of bioreactor culture cells to mitoxantrone. Nine out of 84 genes showed higher expression at four hour post mitoxantrone treatment in cells cultured at rotating condition compared to those at static. Taken together, the results reported here indicate that simulated microgravity may alter the responses of LNCaP cells to mitoxantrone treatment. The alteration of oxidative stress pathways in cells cultured under simulated microgravity conditions may be one of the mechanisms to cause such changes of sensitivity of LNCaP cells to mitoxantrone treatment.